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In Defense of a Social Value Requirement for Clinical Research

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ABSTRACT

Many commentators and guidelines endorse the view that clinical research is ethically acceptable only when it has social value, meaning that it collects data which can be used to improve health. A version of this social value requirement is included in the Declaration of Helsinki and the Nuremberg Code, and is codified in many national regulations. At the same time, there have been no systematic analyses of why social value is a requirement for clinical research. Recognizing this gap in the literature, a recent article by Alan Wertheimer argues that two of the extant justifications for the social value requirement are unpersuasive. Wertheimer concludes, contrary to current regulations and guidelines, that it may be acceptable to conduct clinical research which has no social value. The present paper attempts to assess this conclusion by critically evaluating the ethical and policy considerations relevant to the claim that clinical research must have social value. This analysis finds that the two arguments Wertheimer considers do not, on their own, provide a compelling justification for the social value requirement. However, evaluation of a broader range of ethical and policy considerations supports the standard view that social value is an ethical requirement for the vast majority of clinical trials and should be mandated by guidelines and policies.

(211 words)

1. BACKGROUND

Ethical analyses of clinical research attempt to identify the conditions under which it can be acceptable to expose participants to risks and burdens in order to evaluate medical treatments and interventions. Many analyses conclude that clinical research is acceptable only when it has social value. According to this ‘social value requirement’ (SVR), clinical research that exposes participants to risks and burdens, but lacks social value, is unethical no matter what other positive features it might possess.

Most guidelines for clinical research endorse the SVR.¹ In the words of the Nuremberg Code, clinical research is acceptable only when it has the potential to yield “fruitful results for the good of society.”² Some version of the SVR is also codified in many national regulations. For example, regulations from Kenya maintain that “clinical research must be valuable, meaning that it evaluates a diagnostic or therapeutic intervention that could lead to improvements in health or well-being.”³

1 World Medical Association. 2013. *Declaration of Helsinki: Ethical principles for medical research involving human subjects*. Available at: <http://www.wma.net/en/30publications/10policies/b3/> [Accessed 12 January 2016].

2 The Nuremberg Code. 1949. Available at: <http://www.hhs.gov/ohrp/archive/nurcode.html> [Accessed 12 October 2015].

³ National Council for Science and Technology. 2004. *Guidelines for Ethical Conduct of Biomedical Research Involving Human Subjects in Kenya*. Nairobi, NCST NO. 45. Available at:

Despite this widespread endorsement, there have been surprisingly few analyses of what constitutes socially valuable research,⁴ and almost no systematic analysis of whether in fact social value is a necessary condition for ethically acceptable clinical research.⁵ With this gap in mind, Alan Wertheimer has recently considered two possible justifications for what he calls a “universal and robust” SVR, and finds both of them wanting.⁶ Wertheimer concludes that it may be acceptable to conduct clinical research that has no social value, provided study participants consent and are not exploited.

https://www.healthresearchweb.org/files/Kenya_Guidelines_Ethical_conduct_of_research_involving_human_subjects.pdf [Accessed 22 January 2016].

4 B. Freedman. Scientific Value and Validity as Ethical Requirements for Research: A Proposed Explication. *IRB: Ethics & Hum Beh* 1987; 7-10; J.H.T. Karlawish. Clinical Value: The Neglected Axis in the System of Research Ethics. *Accountab Res* 1999; 255-264; C. Grady. Thinking Further about Value: Commentary On a Taxonomy of Value in Clinical Research. *IRB: Ethics & Hum Beh* 2001; 24: 7-8; D. Resnik. Social Benefits of Human Subjects Research. *J Clin Res Best Pract* 2008; 4: 1-7; M. Habets, J.J.M. van Delden, & A.L. Bredenoord. The Social Value of Clinical Research. *BMC Med Ethic* 2014; 15: 66.

5 D. Shaw & B.S. Elger. The Relevance of Relevance in Research. *Swiss Med Wkly* 2013; 143: w13792.

6 A. Wertheimer. The Social Value Requirement Reconsidered. *Bioethics*. XXXX.

To assess this conclusion, the present paper critically evaluates the ethical arguments and policy considerations relevant to the SVR. Our analysis finds that the two arguments Wertheimer evaluates do not provide a compelling justification for this requirement. However, evaluation of a broader range of ethical and policy considerations provides strong support for the standard view: social value is an ethical requirement for clinical research and should be mandated by policy and regulation.

2. SCOPE OF ANALYSIS

2.1 Defining social value

Clinical research is a subset of research with human participants that focuses on evaluating methods to prevent, treat or cure illness and disease, or on generating the knowledge necessary to develop such methods. We leave to others the question of whether social value is an ethical requirement for research involving human participants more generally, such as economics research that involves playing computer games to learn how humans make decisions under conditions of uncertainty.

We assume the standard conception of social value according to which clinical research has social value to the extent that it collects data which can be used to improve health.⁷ Such data is gained, for example, by evaluating preventive, diagnostic, therapeutic or palliative interventions, or by conducting pathophysiological studies that are necessary to develop such interventions.

⁷ E.J. Emanuel, D. Wendler & C. Grady. What Makes Clinical Research Ethical? *JAMA* 2000; 28: 2701-2711.

This includes studies that identify methods which do not work and thereby point the way to more promising approaches.

The standard conception of social value does not exclude the possibility that clinical research may be socially valuable in ways that do not involve improvements in health. For example, clinical research can provide rewarding careers for scientists, employment for citizens, and a sense of fulfillment for participants. We will bracket these and other types of potential social benefit and assume that clinical research has social value only to the extent that it collects which may be used to improve health.

2.2 Requiring social value

The SVR holds that clinical trials must have the potential to improve health, not that they in fact do so. At least some studies turn out to have essentially no social value at all. For example, some clinical trials end up recruiting so few participants that they yield no useful information. These trials do not violate the SVR, provided there is sufficient reason to believe *ex ante*—at the time the trials are initiated—that they will yield data which can be used to improve health.

Next, the SVR applies to studies, not to the enrollment of specific individuals in these studies. Imagine it is known *ex ante* that the enrollment of a specific individual will not contribute to, nor detract from the social value of a given study. As we will understand it, the SVR does not preclude enrollment of this individual. We also will not consider whether, in some cases, the SVR should be further specified regarding who should benefit, or in what ways. For

example, some guidelines require that research in low-resource settings must be responsive to the health needs of the communities in which it is conducted—in other words, it must have local social value.^{8 9}

Finally, we will not consider how the SVR should be implemented and enforced. Should the evaluation of whether a given study has social value be conducted by regulators or research ethics committees, research advocacy groups or funders—or someone else? And what should the responsible party do in response to studies that lack social value? Discourage them? Prohibit them?

3. ETHICAL AND POLICY ARGUMENTS

The following sections examine eight ethical and policy arguments that, taken together, provide strong support for an SVR.

3.1 Protecting participants who cannot consent

8 Council for International Organizations of Medical Sciences (CIOMS).

International Ethical Guidelines for Biomedical Research Involving Human Subjects. 2002. Available at

http://www.cioms.ch/publications/guidelines/guidelines_nov_2002_blurb.htm.

[Accessed 12 October 2015].

⁹ S. Shah, R. Wolitz & E.J. Emanuel. Refocusing the Responsiveness Requirement. *Bioethics* 2013; 27: 151-159.

There is considerable debate over when it is acceptable to expose individuals who cannot consent to research procedures that do not offer a prospect of clinical benefit (what we refer to as ‘net risk’ procedures). For example, under what conditions (if any) is it acceptable for healthy children to undergo a purely research lumbar puncture in order to establish normal levels for a protein in the cerebrospinal fluid?

Commentators have offered a number of ethical justifications for net risk research with individuals who cannot consent.¹⁰ For present purposes, the important point is that all of these justifications require the research to be socially valuable. For example, some argue that it can be acceptable to enroll children in research involving net risks because it teaches them the value of helping others.¹¹ As mentioned above, there are a number of ways in which clinical research may benefit others. It may help to advance investigators’ careers or realize a profit for the sponsoring company. However important these goals might be in other regards, they seem ill-suited to teaching children the value of altruism. In contrast, children can plausibly learn to appreciate the value of altruism by enrolling in studies that are designed to identify new methods for promoting the health of future patients.

10 Reference withheld for review purposes

11 W. Bartholome. The Ethics of Non-Therapeutic Clinical Research on Children. In: National Commission. *Appendix to Report Recommendations: Research Involving Children* 1977: 3.1-3.22; T.F. Ackerman. Moral Duties of Parents and Nontherapeutic Clinical Research Procedures Involving Children. *Bioethics* 1980; 2: 94-111.

Others argue that essentially everyone has realized benefits to their health as the result of prior net risk research, and everyone—including individuals who cannot consent—therefore has an obligation to participate in such research. This argument makes sense only to the extent that the research in question has the potential to improve health for future individuals.¹² Still others maintain that participating in research with the potential to improve health offers the opportunity to contribute to the valuable activities that may benefit others. Doing so can thereby promote our interest in living a better life overall—even when the research involves some net risks and the participants cannot consent.¹³ In contrast, it is less clear that helping a company profit from a study of questionable social value contributes to a better life overall. In sum, this striking overlap of justifications provides strong support for a social value requirement with respect to net risk research with participants who cannot consent.

3.2 Ensuring the acceptability of high-risk research with competent adults

12 J. Harris & S. Holm. Should We Presume Moral Turpitude in our Children?—Small Children and Consent to Medical Research. *Theor Med Bioethics* 2003; 24: 121-129; D.W. Brock. Ethical Issues in Exposing Children to Risks in Research. *Children as Research Subjects: Science, Ethics and Law* 1994; 81-101.

¹³ Reference withheld for review purposes

Respect for autonomy generally requires us to allow competent adults to make their own decisions and lead their own lives, even when they engage in risky activities that have little or no social value. For example, we should respect the decisions of competent adults to participate in reality TV shows that pose some net risks and have (arguably) no social value. With this in mind, imagine that a researcher proposes to enroll competent adults in a clinical trial that has little, if any social value, but has the potential to earn the sponsoring company a profit —perhaps the study of a drug that is so similar to already approved treatments in terms of side effects, route of administration, cost and so on, that it has no potential to benefit future patients. On what grounds might guidelines or regulations prohibit this study?

Respect for autonomy is important. At the same time, society appropriately limits the activities of even competent adults, especially when it comes to inappropriate and high-risk activities. Reality TV shows that involve competent adults agreeing to swim across rivers and hike in the wilderness without a compass are permitted, but we would not permit a show involving Russian Roulette. Imagine that a TV station proposes a reality TV show, “Firing Squad”, in which competent adults are lined up against a wall. An executioner, equipped with a gun that contains one bullet in its 20 chambers, aims at the group and pulls the trigger. This show should not be permitted, even if the contestants are fully informed and give their voluntary consent, and even if they receive a significant amount of money for participating.

One might cite a number of reasons to prohibit this show. It seems inappropriate to be entertained by possible executions; it might be traumatic to

those who watch it; it might trigger copycat incidents. But, even if all these concerns are addressed—imagine the game is played in private and not televised—it still should be prohibited. Why? Briefly, morality is not exhausted by respect for competent adults’ ability to make their own decisions. It can be appropriate to prohibit an activity because it poses significant net risks and has little redeeming value. For example, it can be appropriate to prohibit entrepreneurs from offering employment to produce something as mundane as fancy dresses under high-risk conditions. In contrast, activities that pose significant net risks, but have important social value are rightly considered ethical, even praiseworthy. For instance, competent consenting adults often are praised for assuming high net risks when fighting fires or safeguarding national security.¹⁴

Although it is difficult to determine precisely where to draw the line between ethical and unethical activities, a plausible heuristic is to consider whether an activity, given its value and the net risks involved, is reasonable from the perspective of an ideal social arbiter.¹⁵ This heuristic provides a standard for determining whether an activity should be prohibited on moral grounds. When fair consideration of all affected parties suggests that the risks of an activity are excessive compared to its potential social benefits, society has strong reason to prohibit it, even when it involves consenting adults. This

¹⁴ Even in these cases, there remains an obligation to reduce the risks where possible, suggesting that the risks of even very valuable research should be reduced as well.

¹⁵ Reference withheld for review purposes

analysis suggests that high net risk research with competent adults should be permitted only when it satisfies the SVR.

3.3 Maintaining researcher integrity

Clinical research does not involve participants merely facing risks; research risks are not analogous to the risk of being attacked by a bear while on a hike. Clinical investigators actively and intentionally expose participants to risks, frequently by invading their bodies to inject investigational agents or remove samples, or by asking sensitive health-related questions. These features raise the question of what constitutes appropriate behavior on the part of investigators.¹⁶

As Alan Wertheimer points out, there is no comprehensive account of appropriate investigator behavior.¹⁷ Wertheimer also highlights the fact that the point of ethical guidance for clinical research is typically understood as protecting participants' rights and interests, not preventing investigators from acting inappropriately. However, the absence of a comprehensive account of appropriate investigator behavior, and the general emphasis on protecting participants, does not imply that limits on investigator behavior must all be grounded in protecting participants.

Imagine a study that involves participants undergoing a lumbar puncture without anaesthetic merely to see how painful it is. Further imagine that participants are fully informed and paid for their participation. This study is

16 Reference withheld for review purposes

17 Wertheimer, XXXX, *op. cit.*

not clearly problematic in the way that a study involving very high net risks would be, analogous to the “Firing Squad” TV show. In particular, given the relatively moderate net risks of a lumbar puncture, it is not clear that this study is unethical in virtue of exposing participants to excessive risks. Yet, research ethics is not just about what happens to participants; it is also about what investigators do to them as moral agents.¹⁸ Investigators should not insert needles into participants’ spinal columns and intentionally inflict pain without a good reason, thus raising the question: When can it be acceptable for investigators to interact with participants in ways that expose them to net risks?

Individuals’ rights to bodily integrity and privacy place strong ethical claims against investigators inserting a needle into participants’ bodies or asking sensitive questions purely for research purposes. However, by giving valid consent, competent adults waive their rights against being so treated. Hence, if there are limits on how investigators can treat consenting adults in the context of net risk research, these limits must have some source other than participants’ rights.

While we do not have a complete (or even partial) account of agent-centered limitations in clinical research, it seems clear that these limits go beyond prohibiting investigators from violating participants’ rights. Investigators also need positive reasons to justify their studies. In the above lumbar puncture study, there needs to be a positive reason why investigators

18 T. Nagel. *Mortal Questions*. 2012. Cambridge, UK: Cambridge University Press.

insert needles into participants' backs, inflicting pain and exposing them to net risks. Absent the potential to benefit participants clinically, the potential to learn something important for improving health provides a clear and strong justification.¹⁹ In this case, an investigator can say: "Yes, I am inserting a needle into your spinal column for research purposes, but I do this as part of a valuable effort to gain information that has the potential to improve the health of future patients." Other possible benefits of conducting clinical trials do not seem to yield a compelling justification for investigators' behavior. For example: "I am inserting this needle into your spinal column in order to earn tenure".

3.4 Avoiding participant deception

Society benefits from clinical research and takes active steps to promote it, primarily through efforts to advance and encourage the view that clinical research is socially valuable. Empirical data suggest that these efforts have been successful. In a recent global survey, 77% of 5701 respondents indicated that individuals who participate in clinical research make a valuable contribution to science and society.²⁰

¹⁹ Emanuel et al, *op. cit.*

²⁰ Center for Information and Study on Clinical Research Participation. 2013). *Perceptions and Insights Study: Public and Patient Perceptions of Clinical Research*. Report on general perceptions. Available at: <https://www.ciscrp.org/wp-content/uploads/2014/01/2013-CISCRP-Study-General-Perceptions.pdf> [Accessed 11 February 2015].

Empirical studies also find that the potential to help future patients is an important reason why many individuals enroll in clinical research, especially in studies that offer no prospect of clinical benefit.²¹ Relying on this motivation to enroll individuals in research that lacks social value involves a kind of deception or fraud. It involves investigators relying on subjects' false belief to get them to enroll in studies that conflict with their clinical interests. The SVR protects participants against this fraudulent behavior by ensuring that net risk studies have the potential to benefit future patients. Moreover, to the extent that society, by promulgating and encouraging the view that clinical research is socially valuable, is responsible for individuals' belief, the SVR protects society from becoming complicit in this fraud.

A different way to avoid participant deception would be simply to inform prospective participants that a given study lacks social value. However, it seems unlikely that investigators would adopt this approach. They likely would be unwilling to admit that their studies lack social value and likely would be concerned that candor in this regard would deter individuals from enrolling. Moreover, as we discuss below, informing participants that *some* studies lack social value may undermine public trust in clinical research *in general*. These considerations suggest that, at least in the world we inhabit, the SVR is a key safeguard against deception in clinical research that poses net risks.

²¹ L. Stunkel & C. Grady. More than the money: a review of the literature examining health volunteer motivations. *Contemp Clin Trials* 2011; 32(2): 342-52.

3.5 Safeguarding against exploitation

The SVR has been cited as an important protection against the exploitation of research participants.²² In response, Alan Wertheimer has argued that the SVR actually increases the potential for exploitation.²³ To make this argument, Wertheimer appeals to his own account, according to which exploitation occurs when a specific transaction places an unfair balance of risks and benefits on one or more of the parties to the transaction.²⁴ On this account, research participants are exploited when they receive an unfair share of the benefits of a study, given the risks and burdens they assume, and the extent to which others benefit from their participation.²⁵ Since the SVR mandates that clinical trials must have the potential to benefit future patients, and there might be millions of them, Wertheimer concludes that it actually increases the chances that participants will be exploited.

Wertheimer's argument makes sense, but only to the extent that one focuses on individual research studies.²⁶ Things look very different when we

²² Emanuel et al, *op. cit.*

²³ Wertheimer, XXXX, *op. cit.*

²⁴ A. Wertheimer. *Exploitation*. Princeton University Press, 1999.

²⁵ A. Wertheimer. *Rethinking the Ethics of Clinical Research: Widening the lens*. Oxford University Press, 2010.

²⁶ Wertheimer's argument also depends on his account of exploitation. For present purposes, we bracket possible criticism of this account and instead

consider clinical research as a cooperative enterprise that is designed, through the conduct of numerous studies over many years, to improve health for all citizens. At this level, the potential for exploitation depends not simply on the distribution of benefits and burdens within a given study, but on the distribution of benefits and burdens across the enterprise as a whole. If participants face net risks and burdens as part of a socially valuable study, but are denied access to the results of research, then contributing to studies with social value can indeed increase the potential for exploitation as Wertheimer claims. In contrast, as part of a collective program to which everyone contributes, and from which everyone benefits, an SVR can reduce the potential for exploitation. It can ensure that clinical research generates benefits for all those who contribute to it

Unfortunately, mechanisms to ensure equitable access to the benefits of clinical research do not exist in all countries, let alone beyond national boundaries, and only a small number of people participate in research studies. This raises concern that, in many places, the SVR represents a less than ideal safeguard against exploitation. This is important because Wertheimer offers a more straightforward approach. He writes: “If payment should be regarded as a benefit, then subjects are not exploited if the payment is sufficient to adequately compensate them for the risks and burdens of participation even if the research is entirely lacking in social value.”²⁷

focus on showing that a SVR is a compelling way of avoiding exploitation—on Wertheimer’s own account—given current research practices.

²⁷ Wertheimer, xxx

While this argument makes sense in theory, it would require what strikes us as an extremely unlikely change in practice. In particular, compensating participants for the risks and burdens they face is not sufficient to avoid exploitation; the level of compensation would also need to take into account the extent to which others benefit from participants' involvement. For example, a series of clinical trials can yield large profits for a company. Obviously, a range of individuals contribute to the successful development of a new intervention, and the claims of all of them would need to be considered in any fair distribution. However, the contributions of research participants can be crucial and their fair share of the profits may be significant. A small number of participants who are instrumental to the development of an intervention that produces tens of billions of dollars in profit might need to receive hundreds of thousands of dollars to ensure a fair transaction.

It seems unlikely, at least in the foreseeable future, that participants will receive this level of compensation. Sponsors would be reluctant to pay participants at this level. And doing so would change in substantial ways how we understand the role of research participants, what it means to obtain their voluntary informed consent, and so on. Uncertainty about these changes likely increases sponsors' reluctance to address the potential for exploitation through payment. This suggests that a SVR represents an important component of what currently appears to be the best (albeit imperfect) approach to addressing concerns about exploiting research participants.

3.6 Stewardship of public resources

Public officials have an obligation to exercise stewardship of public resources by spending them in ways that promote socially valuable goals. This obligation is not specific to research, but applies to public expenditures in general. As mentioned, there are different socially valuable goals that might be promoted by research, such as employment or economic activity. However important they may be, these goals can be realized in other ways. In contrast, clinical research is vital to developing and evaluating interventions that have the potential to improve health. The importance of this goal, and the absence of alternative ways to achieve it, provides strong reason to insist that the approximately 1/3 of all clinical research studies which are publicly funded satisfy an SVR.²⁸

Granting this, Wertheimer points out that “corporations are permitted to spend their resources as they see fit, subject to specific constraints such as not marketing drugs that have not been approved by the regulating agency.”²⁹ This view implies that private companies may use their own resources to fund clinical trials that have no social value, provided the risks are not excessive and participants give voluntary informed consent. This argument overlooks the numerous public contributions to privately funded research. For example, the early phase studies on which many company studies are based are often publicly funded. In addition, much of the infrastructure on which clinical trials

28 J. Chakma, G.H. Sun, J.D. Steinberg, S.M. Sammut & R. Jagsi. Asia's Ascent — Global Trends in Biomedical R&D Expenditures. *N Engl J Med* 2014; 370: 3-6.

29 Wertheimer, XXXX, *op. cit.*

depends, such as the methods that are used in clinical research, trace to public support and funding. Governments also help to train the investigators and clinicians that are needed to run clinical trials, and contribute to the review, approval and reimbursement of the products that are developed through commercial studies. The magnitude of these contributions varies widely and will be low for some studies, as well as difficult to estimate in any precise way. Nonetheless, there remains at least some public support for essentially every privately funded study.

One might argue that governments can provide this support to pharmaceutical companies without insisting on any specific conditions in return. Whether this is right depends on whether doing so is consistent with the obligation to exercise proper stewardship of public resources. Whatever that analysis might suggest, requiring clinical trials to have social value ensures that the provision of these benefits is consistent with appropriate stewardship of public resources. This conclusion does not imply that all clinical research studies should be required to have *significant* social value. Instead, it suggests that all clinical research studies, including those that are (mostly) privately funded, pose low to moderate net risks, and enroll only competent adults, should be required to have *sufficient* social value, where the level of required value is a function of the degree of public contributions that went into the study.

3.7 Promoting public trust

Clinical research provides significant benefits to society. Generation and preservation of these benefits depends on public trust in and support of clinical research.³⁰ With the SVR in place, potential participants can be assured that they will be invited to face the risks and burdens of clinical research only when the studies have the potential to improve health. In this way, an SVR provides an important protection for public trust in clinical research and hence, indirectly, for the enterprise of clinical research itself. In response, Wertheimer points out that the extent to which clinical research depends on public trust is “an empirical question that requires much more investigation.”³¹ However, as he also points out, it is plausible to think that social value is important for public trust in clinical research. The question we face, then, is one of which policy to adopt absent robust data on the importance of public trust.

The potential costs of not requiring social value could be enormous if, in fact, clinical research depends significantly on public trust. In particular, some clinical trials are necessary to achieving fundamentally important goals related to promoting health. For example, identifying effective ways to treat malaria and prevent HIV infection depends on clinical trials. Hence, to the extent that allowing clinical trials which have no social value might undermine trust in and support for these trials, the consequences could be devastating. To see

30 A.J. London. A Non-Paternalistic Model of Research Ethics and Oversight: Assessing the Benefits of Prospective Review. *J Law, Med Ethics* 2012; 40: 930–944.

31 Wertheimer, XXXX, *op. cit.*

this, imagine that sponsors and researchers are permitted to conduct clinical trials that have no social value, provided the net risks are low or moderate and competent adults provide informed consent. We can expect that at least some trials will be conducted for frivolous reasons, for no reason, and even for harmful reasons. In the long run, communities may come to regard clinical research with suspicion and be unwilling to participate. One might hope that permitting both valuable studies and studies that have no social value will not necessarily undermine trust in clinical research in general. For example, investigators and funders might be required to make clear whether a given study has social value, perhaps by placing in bold letters on consent forms: *“This study does not have any potential to help improve health. Instead, it is being conducted to make money for Company X.”* This approach might lead to the public having trust in and supporting those studies that have social value, while regarding studies that have no social value in a different light—for example, as means for employment or earning a profit.³²

This outcome seems possible, but unlikely. Recall that we are limiting the present argument to clinical research defined as a subset of research that focuses on evaluating methods to prevent, treat, and cure illness and disease, or gathering the knowledge necessary for developing such methods. As a result, the average person typically is not in a position to judge whether a given research study justifies the net risks and burdens it poses. Instead, they

³² Moreover, if successful, this approach would also address the potential for participant deception discussed above (section 3.4) without insisting on an SVR.

rely on this being the case, and adoption of an SVR ensures that this is in fact so.

This thought experiment suggests that the potential costs of adopting policies that dispense with a SVR could be significant. How do these costs compare to the potential benefits of doing so? Presumably, the SVR blocks some studies that individuals want to conduct and others are willing to participate in. This is a cost, although likely a very modest one. Beyond this, there are few costs to endorsing an SVR. Even if we did not require that research have social value, we would still need a system to ensure that participants' rights and interests are protected. Given that implementation of the SVR likely can be incorporated into this system with few additional costs, it seems unlikely—albeit an empirical question—that the costs of requiring social value as a matter of policy outweigh the assurance this provides in maintaining public trust.

3.8 Cases versus policies

The argument to this point does not preclude the possibility that there are some studies to which the above arguments in support of a SVR do not apply. In particular, the arguments for requiring social value do not apply to studies that meet all of the following conditions: 1) enroll competent participants who understand that the study has no potential social value; 2) pose no greater than moderate net risks; 3) are consistent with conditions on appropriate investigator behavior; 4) compensate participants commensurate with any net risks and burdens they face and the extent to which their contribution benefits

others; 5) are done in a sufficiently private way; 6) do not use public funds; 7) do not rely on prior studies that were supported by public funds; and 8) do not rely on publicly funded review, approval or reimbursement mechanisms.

Are there studies that satisfy all of these conditions? We are not sure. If such studies exist, social value may not be a requirement for them. However, to the extent that the SVR is part of public policy, it is not clear that these studies matter. Public policies are never fully appropriate for every single case that falls under them. In addition, depending on how complicated it would be, implementation of a system to allow valueless studies might lead to many false positive mistakes—that is, valueless studies that are conducted but should not have been conducted. This provides further reason for the relevant policies to require social value for all clinical research studies.

4. OBJECTIONS AND REPLIES

Critics might argue that the present analysis establishes only that social value (combined with other standard requirements, such as informed consent) is a sufficient condition for ethical clinical research. We have not demonstrated that every possible way of regulating clinical research that does not involve an SVR is ethically problematic. Hence, we have failed to support the standard view that social value is a *necessary* requirement for ethical clinical research.

We admit to not having canvassed every possible way of regulating research without social value and proven that all of them are problematic. If this standard for proving necessity is applied, we have failed to meet it. However, we are not sure—at least in applied ethical reasoning—that anyone

ever meets this standard. In contrast, we do think we have shown that, given the world we live in, and the way that clinical research is conducted in that world, failure to enforce an SVR would lead to problematic studies and overall worse research outcomes. It is in this sense that we conclude that the SVR is necessary for ethical research.

Critics might also argue that our arguments blend ethics and policy, and that it is therefore unclear whether social value is required as a matter of ethics or as a matter of good policy. In our view, it is both, although it can be difficult to draw a clear distinction between the two. Even the argument that most clearly appeals to policy considerations—cases versus policies—has moral salience insofar as it highlights the moral importance of balancing false positive and false negative errors when setting public policy.

5. CONCLUSION

The present analysis identifies eight ethical and policy considerations that together provide strong support for an SVR. Mandating that clinical trials must have (sufficient) social value is important for protecting participants who cannot consent, preventing inappropriate research that poses high net risks, and promoting appropriate investigator behavior. Absent an alternative approach, an SVR also provides some protection against participant deception and participant exploitation. Moreover, an SVR helps to ensure proper stewardship of public resources and promotes public trust and support for clinical research, thereby helping to secure the conditions necessary to continue to improve health. Taken together, these considerations provide

strong support for the claim that social value is an ethical requirement for clinical research and should be mandated by guidelines and policy.

(5029 words)